

Hematopoietic and Lymphoid System Neoplasms

Survival Analysis

BIO392 - Bioinformatics of Sequence Variation

Kim and Sofia, 2022-10-07

Background

Background

Source: <https://doi.org/10.1016/j.immuni.2007.05.012>

NIH

NATIONAL CANCER INSTITUTE

NCI Term Browser

TerminologiesValue SetsMappings

NCI thesaurus

Version:22.08e (Release date:2022-08-29)

C3720

Contains

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Hematopoietic and Lymphoid Cell Neoplasm (Code C27134)

Terms & Properties

Synonym Details

Relationships

Mappings

View All

Terms & Properties

Preferred Name:

Hematopoietic and Lymphoid Cell Neoplasm

Definition:

A neoplasm arising from hematopoietic cells found in the bone marrow, peripheral blood, lymph nodes and spleen (organs of the hematopoietic system). Hematopoietic cell neoplasms can also involve other anatomic sites (e.g. central nervous system, gastrointestinal tract), either by metastasis, direct tumor infiltration, or neoplastic transformation of extranodal lymphoid tissues. The commonest forms are the various types of leukemia, Hodgkin and non-Hodgkin lymphomas, myeloproliferative neoplasms, and myelodysplastic syndromes.

NCI-GLOSS Definition:

A cancer of the blood or bone marrow, such as leukemia or lymphoma.

The diagram illustrates the process of hematopoiesis, showing the differentiation of blood cells from stem cells through committed progenitors and maturing cells. The process is organized into three main stages: Stem cells, Committed progenitors, and Maturing cells.

- Stem cells:** The process begins with a Repopulating cell, which can undergo self-renewal or differentiate into a CFU-s (Colony-Forming Unit-Spleen) or a CMP (Common Myeloid Progenitor).
- Committed progenitors:** The CMP differentiates into a CLP (Common Lymphoid Progenitor) and a MEP (Myeloid Erythroid Progenitor). The CLP further differentiates into a Pre-T cell and a Pre-B cell. The MEP differentiates into a BFU-E (Bursting Unit-Erythroid) and a Meg-CFC (Megakaryocyte Colony-Forming Cell).
- Maturing cells:** The Pre-T cell matures into a T lymphocyte. The Pre-B cell matures into a B lymphocyte, which can further differentiate into a Plasma cell. The BFU-E matures into a CFU-E (Colony-Forming Unit-Erythroid), which then matures into an Erythrocyte. The Meg-CFC matures into a Megakaryocyte, which then matures into Platelets. The GMP (Granulocyte-Macrophage Progenitor) differentiates into an Eo-CFC (Eosinophil Colony-Forming Cell), which matures into an Eosinophil. The GMP also differentiates into a GM-CFC (Granulocyte-Macrophage Colony-Forming Cell), which further differentiates into a G-CFC (Granulocyte Colony-Forming Cell) and an M-CFC (Macrophage Colony-Forming Cell). The G-CFC matures into a Neutrophil, and the M-CFC matures into a Monocyte, which can further differentiate into a Macrophage, Kupffer cell, Langerhans cell, or Dendritic cell. The Mast-CFC (Mast Cell Colony-Forming Cell) matures into a Basophil and a Mast cell.

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Background

	Incidence per 100'000 (USA)	5-Year Relative Survival
Leukemia	14.2	65.7%
Myeloma	7	57.9%
Non-Hodgkin Lymphoma	19.2	73.8%
Hodgkin Lymphoma	2.6	89.1%

Data sources:
<https://seer.cancer.gov>
<https://cancerstatisticscenter.cancer.org>

Survival Analysis on lymphoma.csv

- Study CNVs in samples with mutations in the following genes:
 - TP53-
 - CDKN2A-
 - ERBB2+
 - MYC+

Survival Analysis on lymphoma.csv

- Study CNVs in samples with mutations in the following genes:

- **TP53-** (Godley et al, 2017)

- CDKN2A-

- ERBB2+

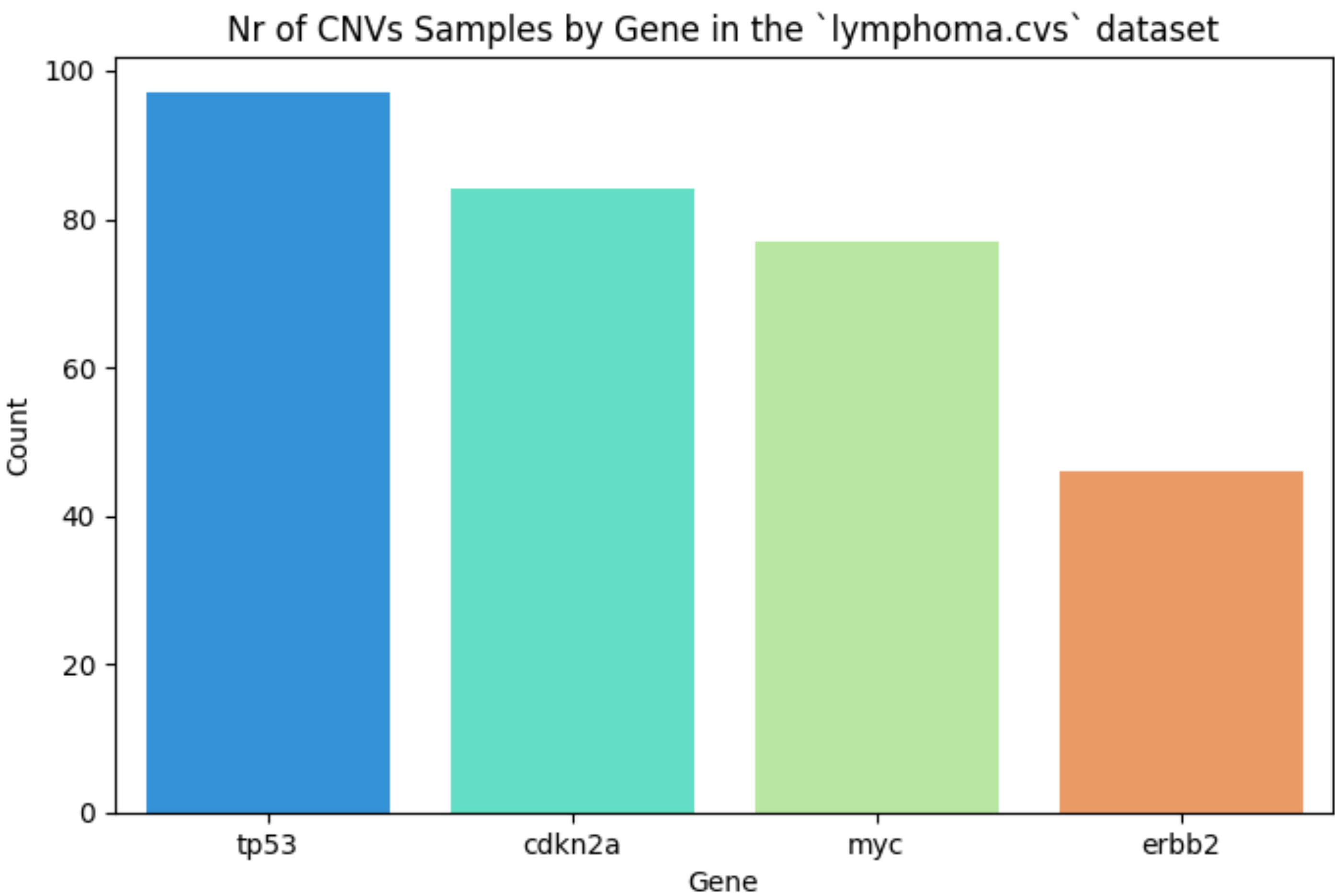
- **MYC+** (Skibola et al, 2010)

Evidence of poor prognosis
in hematopoietic and lymphoid system
malignancies



Dataset

lymphoma.csv



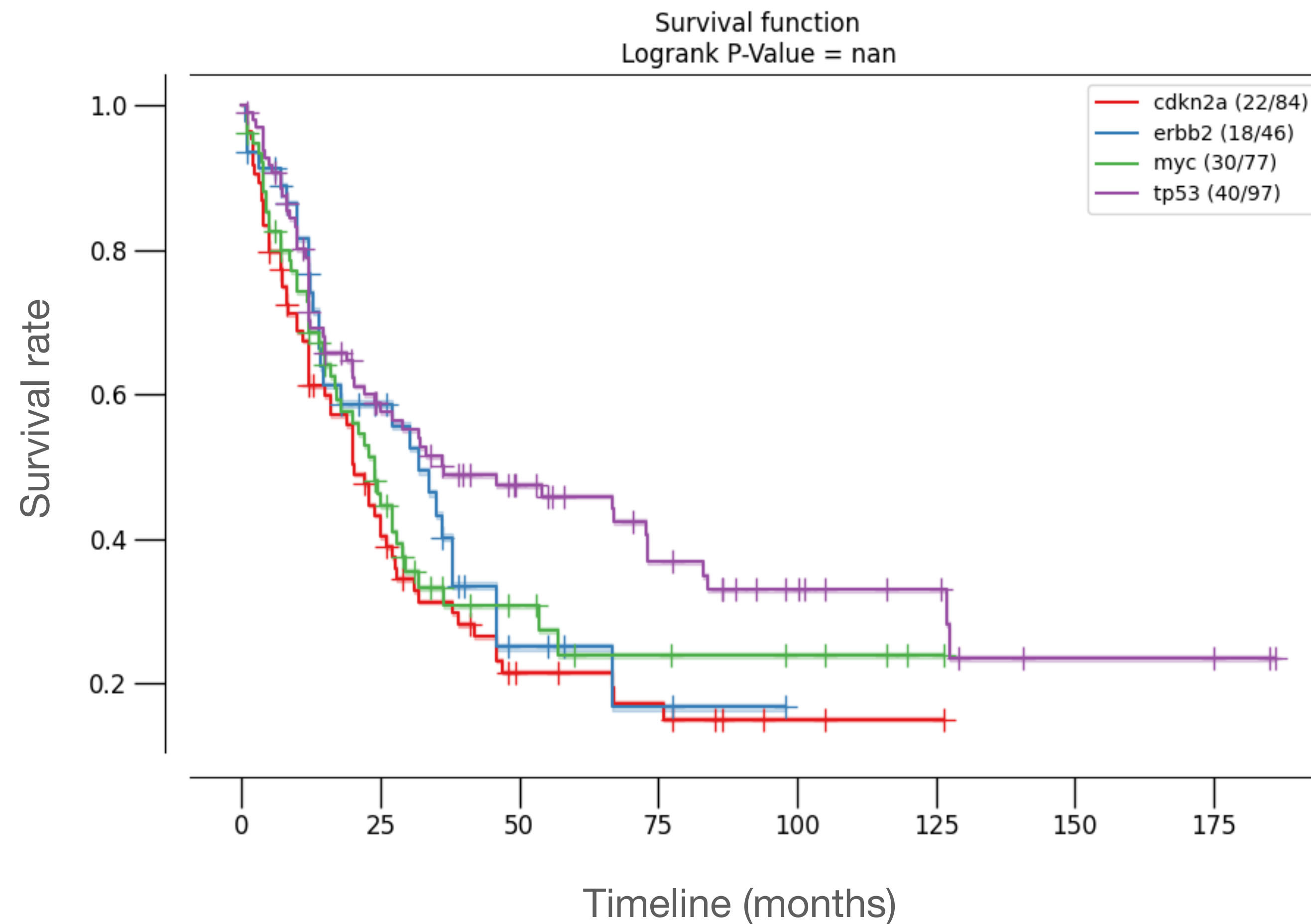
After matching...

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Data columns (total 9 columns):
#   Column                                Non-Null Count  Dtype
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0   info.followupMonths                  237 non-null   float64
1   info.death                          237 non-null   int64
2   group                               237 non-null   object
3   histologicalDiagnosis.id            237 non-null   object
4   info.cnvstatistics.cnvfraction      237 non-null   float64
5   sex                                 237 non-null   object
6   pathologicalStage.label             237 non-null   object
7   info.cnvstatistics.dupfraction      237 non-null   float64
8   info.cnvstatistics.delfraction      237 non-null   float64
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Results

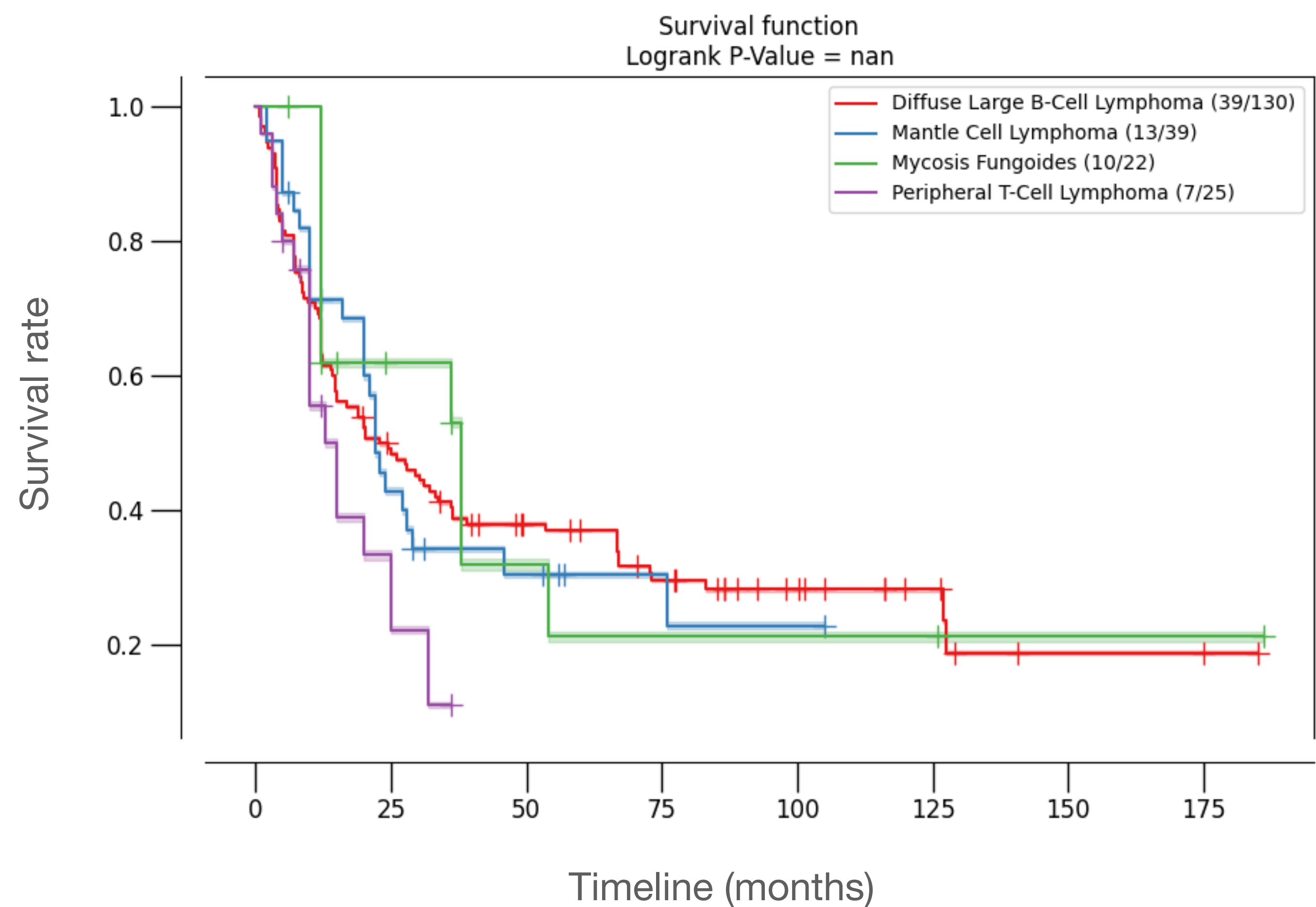
KM Curves

Survival rate based on gene



KM Curves

Survival rate based on tumor type

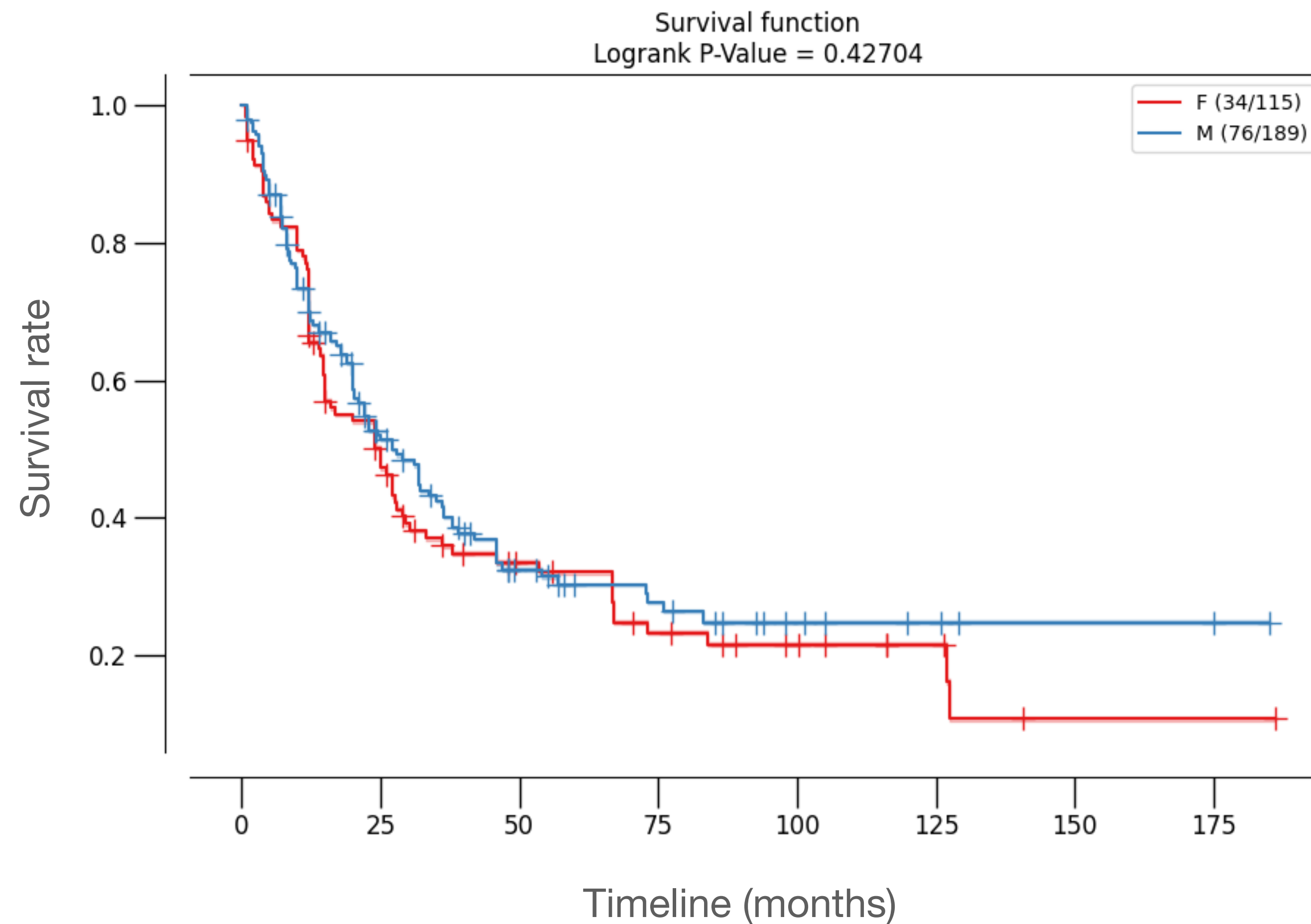


Note 1: plot excluded tumor types with sample size < 5

Note 2: Mycosis Fungoides is also T-cell Lymphoma

KM Curves

Survival rate based on sex of the patient

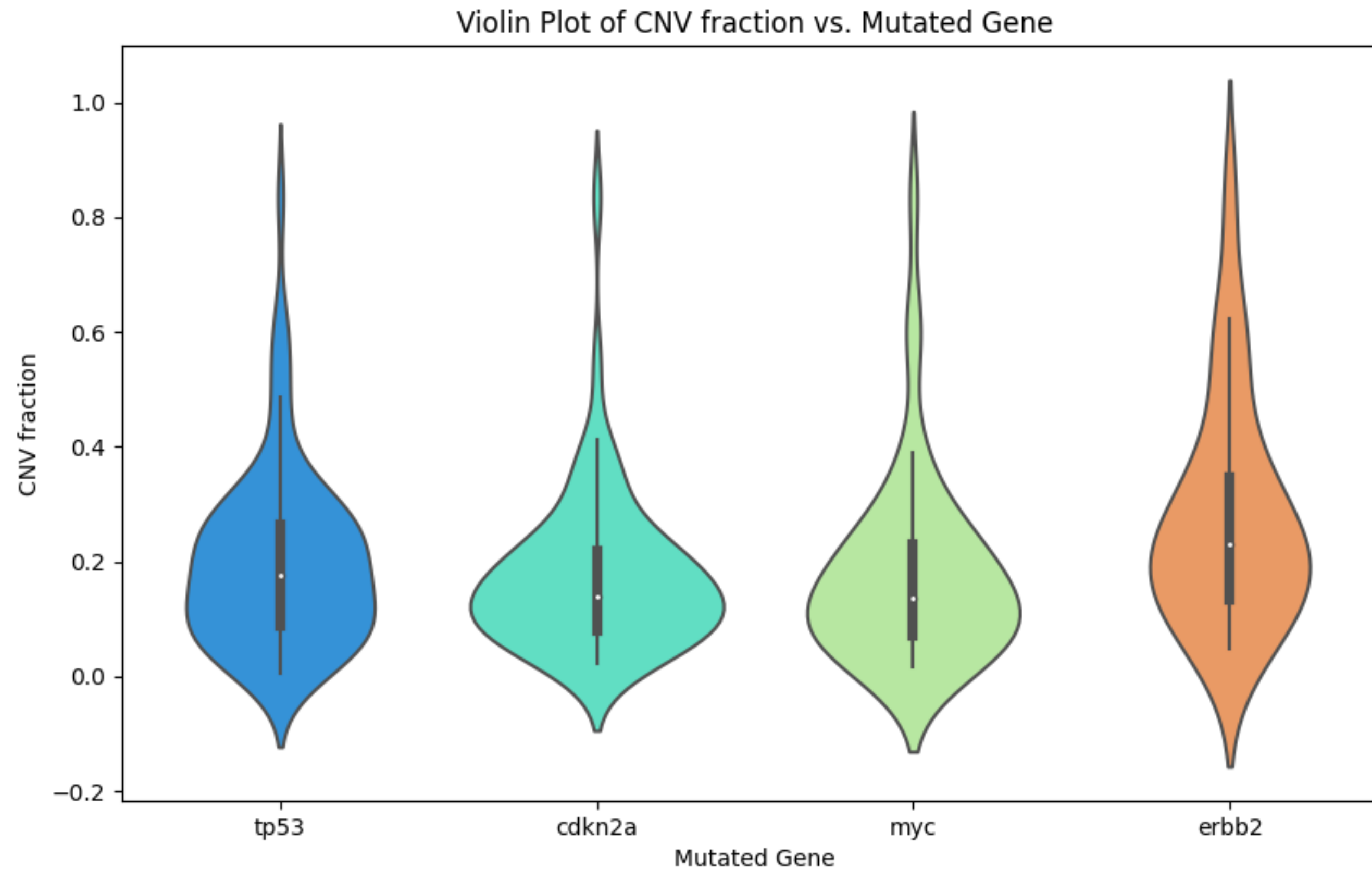


CNV fraction

Does CNV fraction change across samples with different mutated genes?

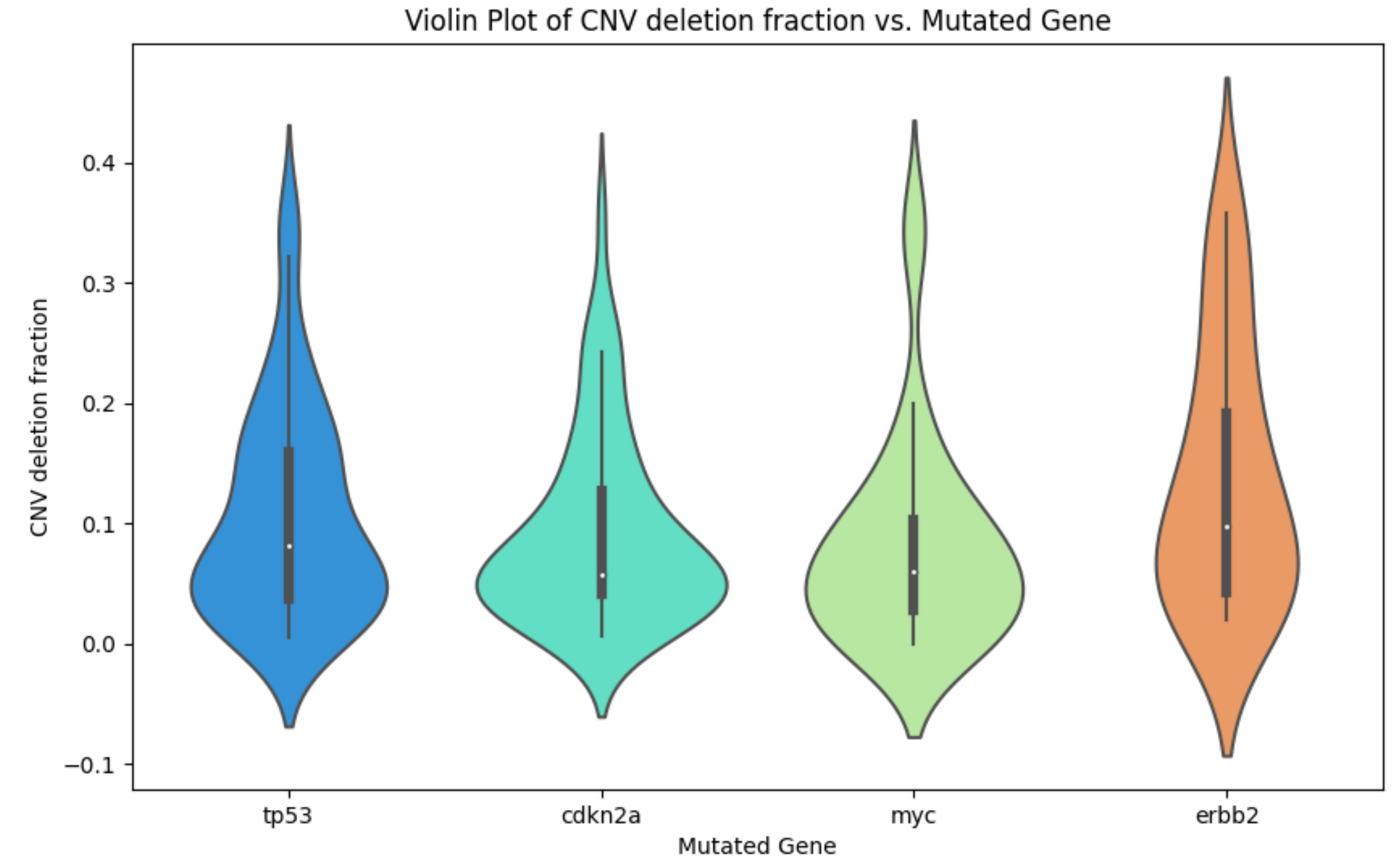
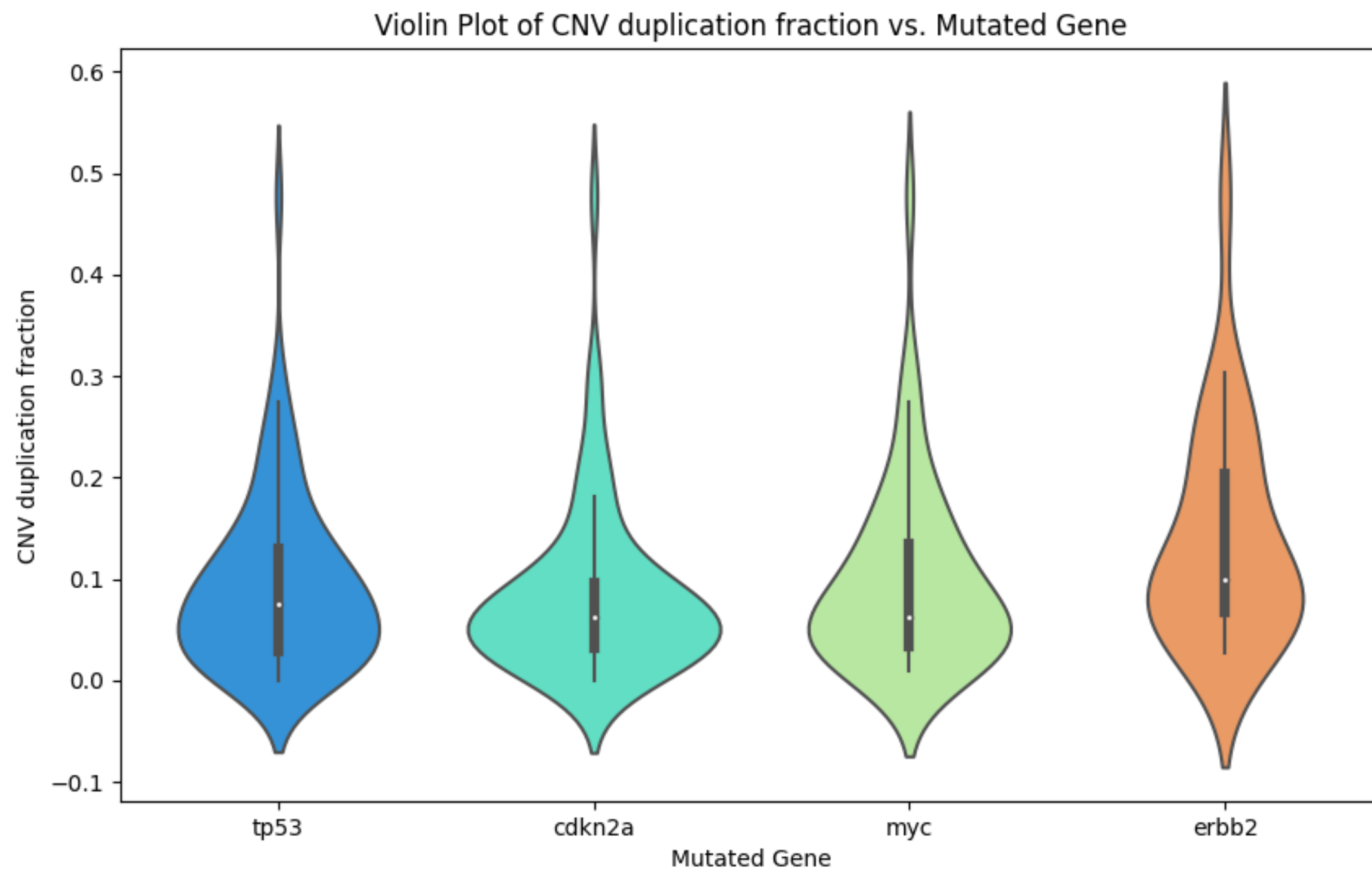
CNV fraction

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CNV fraction

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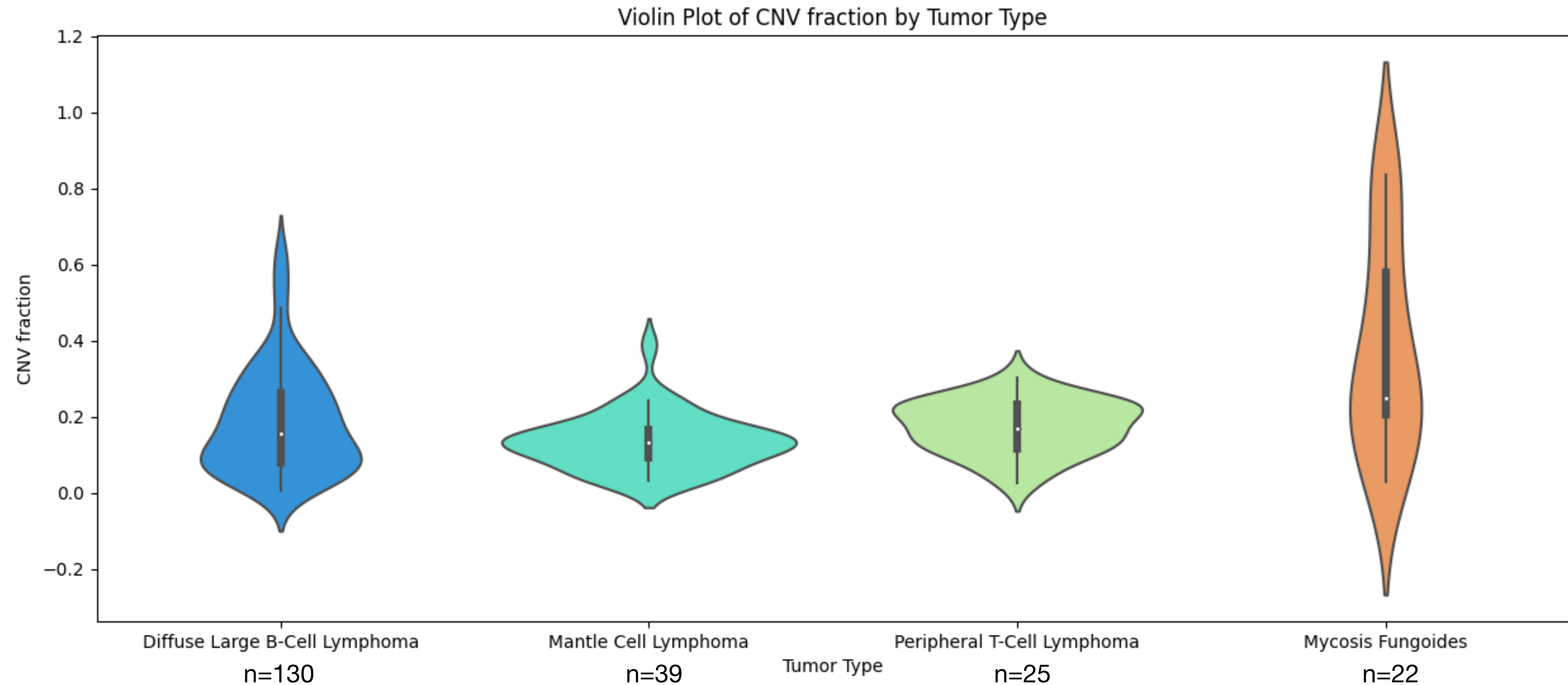


CNV fraction

Does CNV fraction change across tumor types?

CNV fraction

Does CNV fraction change across tumor types?

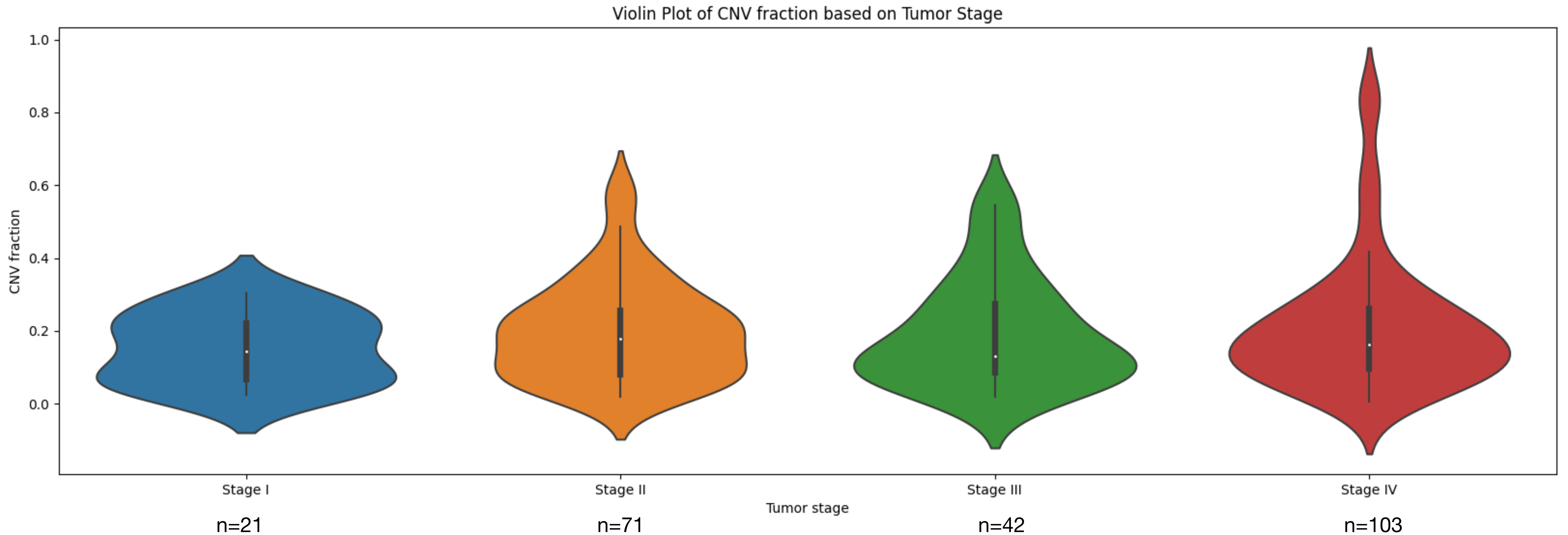


CNV fraction

Does CNV fraction increase with tumor stage?

CNV fraction

Does CNV fraction increase with tumor stage?



Summary

Summary I: survival rate

- (Significant) difference in survival rate depending on the mutated gene
 - ↑ Higher survival rate in patients with TP53 mutations (unexpected - maybe due to small sample size)
- (Significant) difference in survival rate depending on the tumor type
 - Peripheral T-cell lymphoma patients have ↓ lowest survival rate
- No significant difference in survival rate between male and female patients

Summary II: CNV fraction

- CNV fraction has **similar** distributions across the different mutated genes
 - Data indicates CNV fraction of the **whole** genome - not of the single mutated gene
- CNV fraction has **different** distributions depending on tumor types
- CNV fraction is **similar** at all tumor stages
 - Disease progression doesn't seem to cause more CNVs (unexpected)

Comments and Outlook

1. No myeloma (and leukemia) tumor samples: expected ↓ lower survival rate compared to lymphomas
2. Sample size:
 - A. Increase the overall sample size to get more significant observations
 - B. Ensure similar sample sizes when comparing groups
3. Get CNV data for oncogene or TSG sequence instead of working with whole genome CNV data: compare CNV fractions between the genes of interest

**Thank you! :-)
Questions?**

References

Articles

Godley, L. A., & Shimamura, A. (2017). Genetic predisposition to hematologic malignancies: management and surveillance. *Blood, The Journal of the American Society of Hematology*, 130(4), 424-432.

Lopez-Santillan, M., Lopez-Lopez, E., Alvarez-Gonzalez, P., Martinez, G., Arzuaga-Mendez, J., Ruiz-Diaz, I., ... & Martin-Guerrero, I. (2021). Prognostic and therapeutic value of somatic mutations in diffuse large B-cell lymphoma: A systematic review. *Critical Reviews in Oncology/Hematology*, 165, 103430

Skibola, C. F., Curry, J. D., & Nieters, A. (2007). Genetic susceptibility to lymphoma. *Haematologica*, 92(7), 960.

Webpages

<https://seer.cancer.gov>

<https://cancerstatisticscenter.cancer.org>

<https://ncit.nci.nih.gov/ncitbrowser/>

<https://progenetix.org>